Global epigenomic reconfiguration during mammalian brain development.

Journal: Science

Publication Year: 2013

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PubMed link: 23828890

Funding Grants: Generation of regulatory T cells by reprogramming

Public Summary:
DNA methylation is implicated in mammalian brain development and plasticity underlying learning and memory. We report the genome-wide composition, patterning, cell specificity, and dynamics of DNA methylation at single-base resolution in human and mouse frontal cortex throughout their lifespan. Widespread methylome reconfiguration occurs during fetal to young adult development, coincident with synaptogenesis. During this period, highly conserved non-CG methylation (mCH) accumulates in neurons, but not glia, to become the dominant form of methylation in the human neuronal genome. Moreover, we found an mCH signature that identifies genes escaping X-chromosome inactivation. Last, whole-genome single-base resolution 5-hydroxymethylcytosine (hmC) maps revealed that hmC marks fetal brain cell genomes at putative regulatory regions that are CG-demethylated and activated in the adult brain and that CG demethylation at these hmC-poised loci depends on Tet2 activity.

Scientific Abstract:
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